ORIGINAL STUDY

Frequency of hypotension in a historical cohort of anaesthetised dogs undergoing elective desexing

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ABSTRACT

The aim of this study was to determine the frequency of hypotension (based on mean arterial pressure measurements; MAP) in healthy dogs that were anaesthetised for elective desexing at Murdoch University Veterinary Hospital (MUVH). The secondary aim was to explore any association between gender, age, body mass, heart rate and anaesthetic induction agent with MAP. We hypothesised that MAP less than 60 mmHg would occur in at least 40% of healthy anaesthetised dogs. A historical cohort study was performed using anaesthetic records from dogs desexed by clinicians in the general practice service at MUVH between 2007 and 2011. Each dog was categorised according to the following criteria: I) hypotension - the lowest MAP present for at least two consecutive measurements was less than 60 mmHg, II) mild hypotension - the lowest MAP present for at least two measurements was between 60–79 mmHg and III) normotension - all MAP measurements were between 80–120 mmHg. The frequency of each category (point estimate, 95% confidence interval - CI) was calculated. Records from 188 dogs were included with 87/188 (0.46; 95% CI 0.39-0.53) categorised as hypotensive, 72/188 (0.38; 95% CI 0.31-0.45) as mildly hypotensive and 29/188 (0.15; 95% CI 0.10-0.21) as normotensive. Normotensive dogs were significantly older than hypotensive and mildly hypotensive dogs (P=0.0003 and 0.009 respectively) and hypotensive dogs had significantly lower body mass than mildly hypotensive dogs and normotensive dogs (P=0.008 and P=0.015 respectively). The frequency of hypotension was significantly higher when acepromazine and methadone was administered compared to acepromazine and morphine. The frequency of hypotension observed in the current study was at least as high as hypothesised at approximately 40%. This supports the concern that the development of hypotension is not infrequent and monitoring and managing blood pressure in healthy dogs is important. The significantly higher frequency of hypotension in younger and smaller dogs suggests modification of anaesthetic techniques may be warranted. *Aust Vet Pract* 2013;43(2):414-419

INTRODUCTION

The frequency of anaesthetic related mortality in healthy (American Society of Anesthesiologists - ASA I) dogs has been reported to be 0.05%[1], 0.067%[2] and 0.12%.[3] Major causes of perioperative death in small animals include cardiovascular complications.[1,4] Hypotension is reported to be the most common cardiovascular complication observed during small animal anaesthesia.[1,4,5] Currently there are limited studies investigating hypotension in small animals. These studies demonstrate a wide variation in frequency of hypotension from 7%[5] to 37.9%.[4] Reasons for the wide variation between these studies are not readily apparent. Both studies included animals that received different types of anaesthetic drugs and underwent a variety of procedures. The contribution of these different factors to the development of hypotension was not investigated. In addition, these studies included animals with a wide variety of ASA classifications and the effect of this on the frequency of hypotension was also not assessed.

Assessment of the association of hypotension in small animals with ASA scoring may be helpful in developing anaesthetic protocols. Investigation of the contribution of animal factors and different anaesthetic agents to the frequency of hypotension is needed. This information can then be used to develop anaesthetic techniques that will reduce the frequency of hypotension in anaesthetised animals.

The aim of the study was to identify the lowest mean arterial pressure (MAP) recorded during anaesthesia of healthy dogs (ASA I) undergoing elective desexing and estimate the frequency of hypotension (MAP <60 mmHg), mild hypotension (MAP 60–79 mmHg) and normotension (MAP 80–120 mmHg). It was hypothesised that at least 40% of healthy anaesthetised dogs at MUVH would be categorised as hypotensive. An additional aim was to explore any difference in age and body mass across MAP categories or any association between animal factors such as gender and agents used for premedication and induction of anaesthesia, with MAP. The presence of abnormalities in other physiologic variables such as heart rate and temperature was also recorded.

MATERIALS AND METHODS

Anaesthetic records

Anaesthetic records from healthy dogs (ASA I) undergoing anaesthesia for elective desexing in general practice at MUVH between 2007 and 2011 were reviewed. Information obtained from anaesthetic records included the signalment (gender, age and body mass), type and dose of premedicant, and the type and dose of induction agent used.

Premedication included acepromazine (ACP2, Ceva Animal Health) combined with morphine (Hospira Australia) or methadone (Ilium methadone - Troy Labs). Anaesthetic induction agents included propofol (Fresofol 1% - Fresenius Kabi Australia), alfaxalone (Alfaxan, Jurox) and diazepam (Ilium diazepam, Troy Labs) combined with ketamine (Parnell Australia). The maintenance anaesthetic agent used in all cases was isoflurane (ISO, Veterinary Companies of Australia) in 100% oxygen.

Data for blood pressure and heart rate was also retrieved from the anaesthetic records. The blood pressure and heart rate had been recorded using the Surgivet V9203 multivariable monitor (Polymount GCX® Corporation, CA, USA). The Surgivet measures arterial blood pressure using the non-invasive oscillometric technique.

Data analysis

The dogs in this study were categorised according to the following criteria: I) hypotension - the lowest MAP recorded on the anaesthetic record for at least two consecutive measurements was <60 mmHg; II) mild hypotension - the lowest MAP recorded for at least two consecutive measurements was between 60–79 mmHg; and III) normotension - all MAP measurements were between 80–120 mmHg. As oscillometric methods for measuring blood pressure can be affected by animal and environmental factors, two consecutive measurements were used to define the categories to increase the likelihood that the measurement reflected the true physiologic state of the animal. Since physiologic variables were noted on the anaesthetic record at five minute intervals, this equated to at least 10 minutes. The criteria used to define each category was based in part on published normal and abnormal blood pressure measurements.[6-9] Hypotension was defined as MAP <60 mmHg since this is the value that is consistently reported to increase the risk of organ damage, particularly the kidneys. Normotension was defined using the reported reference interval for conscious dogs. Mild hypotension was defined between the minimally acceptable value of 60 mmHg and the lower end of normal at 80 mmHg. Mild hypotension was included as any decrease in MAP below normal will result in a decrease in renal blood flow[10] although the clinical implications of these decreases on organ function have not been established. The proportion of dogs within each MAP category was the response of interest and the point estimate and the 95% confidence interval (CI) was calculated using methods for proportions. Statistical software (SAS v9.3, SAS Institute, Cary, NC) was used for the calculations.

For hypotensive and mildly hypotensive dogs, the heart rate was calculated as the mean of the heart rate measurements that coincided with the MAP measurements used to define the blood pressure category. The mean heart rate recorded at this time was calculated and then categorised according to the following criteria based on published normal and abnormal heart rates[5,11]: I) low - heart rate <80 beats per minute (bpm); II) normal - heart rate 80–150 bpm; III) high - heart rate >150 bpm. For dogs that remained normotensive throughout the anaesthetic, heart rates recorded for the duration of anaesthesia were assessed to determine if the heart rate was observed to fall into one of the above categories for two or more consecutive readings. If the heart rate varied, for example, normal and low heart rate for more than two consecutive readings, the dog would be included in the low heart rate category. The same protocol was used if the dog had normal and high heart rate during the procedure; the dog would be included in the high heart rate category.

Age and body mass were summarised for each MAP category as median and range. The age and body mass were compared across categories using the Kruskal-Wallis rank sum test with the two-sided null hypothesis of no difference rejected at $P<0.05$. Post-hoc comparisons across MAP categories were made using the Kruskal-Wallis procedure with significance determined at a Bonferroni-adjusted $P<0.017$. The MAP categories were stratified according to possible explanatory variables including gender, heart rate, premedicant and induction agent. The proportion of dogs in each MAP category was reported across the explanatory strata. The association between the possible explanatory variables and MAP category was explored using univariate analysis. A Fisher's exact test was performed for each explanatory variable with the two-sided null hypothesis of no association rejected at $P < 0.05$. The doses of premedicants and induction agents across body mass (kg) was graphed for visual assessment of any dispersion. Statistical software (SAS) was used for the analyses.

RESULTS

A total of 188 anaesthetic records from healthy dogs desexed in the general practice at MUVH between 2007 and 2011 were suitable for inclusion. A total of 87/188 (0.46; 95% CI 0.39-0.53) dogs were categorised as hypotensive, 72/188 (0.38; 95% CI 0.31-0.45) dogs were categorised as mildly hypotensive and 29/188 (0.15; 95% CI 0.10-0.21) dogs were categorised as normotensive.

There was a significant difference between MAP categories for age ($P=0.001$) and body mass ($P=0.008$). Normotensive dogs were significantly older than hypotensive and mildly hypotensive dogs ($P=0.0003$ and 0.009 respectively). Dogs with hypotension had significantly lower body mass than dogs with mild hypotension ($P=0.008$) (Table 1).There was no association of gender with MAP categories ($P=0.319$).

All 188 dogs included in this study received acepromazine in combination with a μ opioid agonist. The opioid agonists were morphine in 133 dogs and methadone in 55 dogs. Premedication was administered by intramuscular injection before induction of anaesthesia in all dogs. There was a significant association of premedicant and MAP category ($P=0.012$). There was a significantly higher frequency of administration of methadone and acepromazine in hypotensive dogs and significant lower frequency in normotensive dogs (Tables 2 and 3). There was considerable variation of the dose of acepromazine across body mass (Figure 1).

Out of 188 anaesthetic records reviewed, the anaesthetic induction agent was recorded in 142 records and 110/142 dogs (0.77) received propofol, 12/142 (0.08) received alfaxalone and

Table 1. Signalment (gender, age and body mass) of 188 healthy dogs undergoing desexing. Dogs were categorised according to mean arterial pressure recorded during anaesthesia (hypotension, MAP <60mmHg; mild hypotension, MAP 60-79mmHg; normotension, MAP 80-120mmHg). Frequencies are reported with proportions in parentheses and age and mass are summarised as median (range). *Indicates significantly different from other MAP categories (P<0.017, Bonferroni-adjusted)

		Hypotension	Mild hypotension	Normotension	Total
Gender	All	87 (0.46)	72 (0.38)	29 (0.15)	188
	Male	31 (0.53)	21 (0.36)	6 (0.10)	58 (0.31)
	Female	56 (0.43)	51 (0.39)	23 (0.18)	130 (0.69)
Age (months)	All	6 (6-91)	7 (6-70)	12 (6-60)*	
	Male	7 (6-84)	9 (6–49)	24 (7–60)	
	Female	6 (6-91)	7 (6–70)	12 (6–48)	
Body mass (kg)	All	9.6 (1.5-30.2)*	13.8 (2-30.5)	7.2 (3.3-27.9)	
	Male	7.6 (3.3–27.5)	10.8 (2–30)	8 (3.3–22.7)	
	Female	11.8 (1.5–30.2)	14.2 (2.3–30.5)	7 (3.7–27.9)	

Table 2. Anaesthetic drugs (premedicants and induction agents) used and heart rate of 188 healthy dogs undergoing desexing. Dogs have been categorised according to mean arterial blood pressure recorded during anaesthesia (hypotension, MAP<60mmHg; mild hypotension, MAP 60-79mmHg; normotension, MAP 80-120mmHg). Frequencies are reported with proportions in parentheses. bpm = beats per minutes

		Hypotension	Mild hypotension	Normotension	Total
Premedicant	ACP+morphine	54 (0.41)	53 (0.40)	26 (0.20)	133 (0.71)
	ACP+ methadone	33 (0.60)	19 (0.35)	3 (0.05)	55 (0.29)
	Number of records	87	72	29	188
Induction agent	Propofol	52 (0.47)	37 (0.34)	21 (0.19)	110 (0.77)
	Alfaxalone	5 (0.42)	7 (0.58)	0	12 (0.08)
	Diazepam/Ketamine	11 (0.55)	7 (0.35)	2 (0.10)	20 (0.14)
	Number of records	68	51	23	142
Heart rate (bpm)	Normal (80–150)	62 (0.42)	60 (0.41)	25 (0.17)	147 (0.78)
	High (>150)	23 (0.61)	11 (0.29)	4 (0.11)	38 (0.20)
	Low (<80)	2	1	0	3
	Number of records	87	72	29	188

20/142 (0.14) received diazepam/ketamine (Table 2).There was no significant association between induction agent and MAP category (P=0.252). Collapsing induction categories to propofol versus other showed no association with MAP category (P=0.130). Only 3/188 (0.02) dogs had a heart rate <80 bpm and two of these dogs were hypotensive. No association was found between heart rate and MAP category (P=0.142). Measurements of body temperature were incomplete with only 27 records containing information on body temperature and in the majority of these cases, temperature was only measured at the end of surgery. No statistical analysis was performed on the body temperature data.

Table 3. Median (range) dose of premedicants and induction agents (mg/kg) used for 188 healthy dogs undergoing desexing. Dogs have been categorised according to mean arterial blood pressure recorded during anaesthesia (hypotension, MAP<60mmHg; mild hypotension, MAP 60-79mmHg; normotension, MAP 80-120mmHg). ACP = acepromazine

			Hypotension n = 87	Mild hypotension n = 72	Normotension n = 29
Premedicant	ACP+Morphine	ACP	0.04 (0.01–0.09)	0.05 (0.01–0.09)	0.05 (0.01–0.09)
		Morphine	0.3 (0.1–0.4)	0.3 (0.2–0.4)	0.3 (0.07–0.5)
	ACP+Methadone	ACP	0.05 (0.02–0.07)	0.05 (0.02–0.08)	0.04 (0.04–0.07)
		Methadone	0.3 (0.08-0.4)	0.3 (0.3–0.4)	0.3 (0.3–0.4)
Induction agent	Propofol		3.5 (1–6)	3.4 (2–7)	3.8 (1–7)
	Alfaxalone		1.6 (1–2)	1.3(1–2)	-
	Diazepam+Ketamine	Diazepam	0.2 (0.1–0.3)	0.3 (0.1–0.2)	0.2(0.1–0.2)
		Ketamine	4 (2-6)	4 (3-5)	4(3-4)

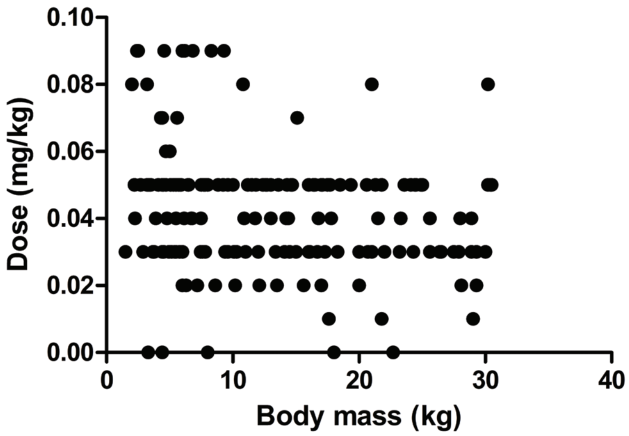

Figure 1. Dose of acepromazine (mg/kg) across body mass (kg) in 188 healthy dogs undergoing desexing.

DISCUSSION

This study reviewed 188 anaesthetic records from dogs desexed in the general practice at MUVH between 2007 and 2011. Using specific criteria for assessing blood pressure, we found a frequency of hypotension at least as high as the hypothesised estimate of 40%. Only a small proportion of dogs remained normotensive during anaesthesia. Mean arterial blood pressure less than 60 mmHg is associated with inadequate perfusion of vital organs such as kidney and brain.[5-7,9] It is concerning that such a large number of dogs had blood pressure measured below 60mmHg in the current study and that very few dogs had normal blood pressure. Although a MAP between 60–79 mmHg is usually considered sufficient to prevent serious organ damage during anaesthesia, there is a linear decrease in renal blood flow as blood pressure decreases within this range.[8,10] Thus, discounting blood pressure within this range as not harmful is possibly careless and it should be interpreted as having potential to reduce organ function.

Our estimated proportion of dogs with hypotension is much higher than a previous report of 7% (179 of 2,556) of anaesthetised dogs.[5] This discrepancy may be due to the different definitions of hypotension used, the method used to measure arterial blood pressure, differences in animal characteristics, drugs used and procedures performed. Gaynor[5] defined hypotension as MAP less than 60 mmHg or systolic arterial blood pressure less than 80 mmHg and did not specify the duration of the decrease in blood pressure measurement. In our study, hypotension was defined as MAP less than 60 mmHg for 10 minutes or more. This is a strict definition compared to other studies and unlikely to have resulted in overestimation.

Gaynor[5] used both the Doppler and invasive blood pressure techniques to measure blood pressure. In anaesthetised dogs, the Doppler technique is reported to overestimate systolic arterial pressure compared to invasive measurements.[12] This could result in a false diagnosis of normotension in some dogs and could have contributed to the lower frequency of hypotension reported in that study. Unfortunately, those authors did not indicate how many measurements were obtained using the Doppler and thus it is not possible to ascertain the influence this may have had on the estimation of the frequency of hypotension in their study. In our study, the Surgivet V9203 was used to measure blood pressure non-invasively via the oscillometric technique. This method can underestimate MAP compared to invasive measurements[13] and may have overestimated hypotension. However, the frequency of hypotension reported in 485 (37.9%) dogs undergoing several types of procedures was similar to that in our study despite using various techniques for measuring blood pressure.[4] This suggests that the method for measuring blood pressure may not be the sole cause of differences between studies.

Other factors that could contribute to discrepancies in the frequency of hypotension reported could include variations in animal characteristics, drugs used and procedures performed. Our study investigated hypotension in young healthy dogs undergoing routine desexing procedures. In contrast, previous studies included animals with variable ASA classification, ages and procedures. Unfortunately, the effect of these different characteristics on frequency of hypotension was not determined thus preventing comparisons between studies.

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Animal factors explored in our study included age and body mass which were significantly associated with MAP category. The frequency of hypotension was significantly higher in younger animals. This is consistent with results of studies investigating hypotension in anaesthetised people.[15] Hypotension during anaesthesia of ASA I patients demonstrated a higher frequency of hypotension during anaesthesia of children than adults.[14] The higher frequency of hypotension in younger animals may be attributed to an immature cardiovascular system. Cardiac contractility and thus cardiac function is reported to increase in dogs from three to nine months of age.[16] This is comparable to the median age of the dogs in the hypotensive and mildly hypotensive categories which were six to seven months and six to nine months, respectively. This immaturity in development of the cardiovascular system reduces the ability of younger animals to compensate for decreases in arterial blood pressure.[15-18]

The body mass of dogs was also found to be significantly associated with MAP category. The body mass of dogs with hypotension was significantly lower than body mass of dogs with mild hypotension. This finding may reflect confounding effects of drug dose administered on a dose per kg rather than a dose per m^3 body surface area. There was considerable disparity in the dose of acepromazine administered to dogs with different body mass with many smaller animals getting some of the highest doses of acepromazine. Acepromazine causes dose-dependant decreases in blood pressure[19,20] and higher doses may have contributed to the higher frequency of hypotension in dogs with low body mass. The dose used may have been influenced by confounding factors such as temperament, breed, type and duration of procedure. It has been reported that the effects of acepromazine on the cardiovascular system are influenced by temperament.[22] Greater decreases in blood pressure have been reported in anxious animals receiving acepromazine when compared to calm animals. This is attributed to the increase in circulating catecholamines that occur in stressed animal which exacerbate the peripheral vasodilation associated with acepromazine.[21,22]

When the type of drugs used for premedication were investigated it was found that the administration of acepromazine and methadone was associated with a higher proportion of hypotensive dogs and lower proportion of normotensive dogs when compared to acepromazine and morphine. Possible reasons could include differences in the effect of methadone and morphine on the cardiovascular system and or differences in the doses of the different agents that were used. Administration of intravenous methadone is reported to cause a significant greater decrease in blood pressure than intravenous morphine in conscious[23] and anaesthetised[24] dogs. However, this decrease in blood pressure is associated with a decrease in heart rate (and cardiac index). Of note, although the decrease in blood pressure was greater following intravenous methadone, none of the dogs developed hypotension defined as MAP less than 60 mmHg.[23,24] In our study, records were not assessed for decreases in heart rate from baseline, however heart rate was defined as above or below normal. Bradycardia defined as heart rate less than 80 bpm was observed in only two of the hypotensive animals making it less likely that bradycardia associated with administration of methadone was responsible for the higher frequency of hypotension observed in dogs receiving this combination. The lack of apparent influence of methadone on heart rate in the current study could be explained by administration of methadone intramuscularly which would be expected to produce lower peak serum concentrations and a less profound decrease in heart rate. The changes associated with these premedicant protocols may reflect variations in the acepromazine dose as explained previously.

There was no significant association of induction agent with MAP category. This is consistent with recent studies in dogs that failed to detect significant differences in cardiovascular function when anaesthesia was induced and maintained with propofol or alfaxalone[25-28] orpropofol or diazepam/ketamine.[29] It is important to point out that, in the current study, a relatively small number of dogs received alfaxalone and diazepam/ketamine for induction of anaesthesia compared to dogs receiving propofol. Data from a larger number of dogs receiving each of the different induction agents is needed to confirm the findings of this study.

To interpret the results of this study it is important to understand the limitations of its design. The main limitation of this study was the use of the oscillometric method for measuring arterial blood pressure. The oscillometric technique is reported to underestimate blood pressure[13,30] which could have overestimated the frequency of hypotension. However, our requirement for a recording over 10 minutes was quite restrictive so may have tempered this possible overestimation. Studies using direct methods of measuring blood pressure are advised to confirm the findings in this study. Other limitations of this study was the reliance of historical data and the large number of confounding variables that are likely present which cannot be clearly accounted for.

This study reports the frequency of hypotension in healthy dogs undergoing elective desexing in general practice at Murdoch University Veterinary Hospital was at least as high as 40%. This high frequency of hypotension justifies monitoring blood pressure during anaesthesia in healthy dogs. Factors that influenced the frequency of hypotension were age, body mass and type of premedicant used. Prospective studies using standardised anaesthetic protocols and direct methods of blood pressure monitoring would be worthwhile to further investigate the role of explanatory factors.

ACKNOWLEDGMENTS

The authors acknowledge the support of the General Practice Section at Murdoch University Veterinary Hospital. This study contributes in part, to the first author's Master of Philosophy thesis, supported by Murdoch University Research Scholarship.

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